REMARKS

Claims 45 to 55 are pending in the application. Claim 55 has been withdrawn from consideration in view of the Examiner's restriction requirement. Because the eight compounds listed in claim 55 are entirely within the scope of claims 45 and 46 and exactly the same as the compounds listed in claims 47, 49 and 52, all of which have already been examined, if claims 45 to 54 are found allowable, applicants respectfully request rejoinder of claim 55.

Claims 45-54 are rejected under 35 U.S.C. 103(a). Applicants request reconsideration and withdrawal of the rejection for the reasons set forth herein.

I. The Rejection of Claims 45 to 54 under 35 U.S.C. 103(a).

Claims 45-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Ajito et al.* (WO 99/38849, US 6,451,800), in view of *Ayal-hershkovitz et al.* (WO 02/060374) and *Raeymaekers et al.* (US 4,859,684) because, in the opinion of the Examiner, both Ajito et al. and Ayal-hershkovitz et al. teach the treatment of thrombocytopenia using benzimidazole compounds and "reasonably suggest" the same use of benzimidazole compounds such as those taught by Raeymaekers et al. because the compounds belong to the same art recognized class.

Applicants contend that "reasonably suggest" is not the proper standard for obviousness under section 103. An invention is obvious if one of ordinary skill in the art would consider it logical to anticipate with a high degree of probability that a trial of it would be successful. *In re Pantzer et al.* 144 USPQ 415.

Applicants newly discovered compounds are agonist of the TPO receptor. Upon agonizing the TPO receptor the target cells produce platelets. The resultant increase in platelet count treats disease states wherein low platelet count is an indication, or thrombocytopenia.

The Examiner cites Ajito et al. as teaching benzimidazole compounds in the treatment of thrombocytopenia. This is simply not the case. In fact Ajito et al. teaches the exact opposite. The benzimidazole compounds of Ajito et al. are indicated as having άvβ3 antagonist, GP IIb/IIIa antagonist and/or platelet aggregation **inhibitory** activity. The compounds of Ajito et al. are blood thinners. They hinder or prevent platelet activity so that clots or platelet thrombosis do not form or are broken up. The compounds of Ajito et al. are given to people who want to decrease platelet activity. Applicant's compounds are given to people who have low platelet count, people who want to increase platelet activity.

The Examiner cites *Ayal-hershkovitz et al.* as teaching benzimidazole compounds in the treatment of thrombocytopenia. The compounds of *Ayal-hershkovitz et al.* are indicated as heparanase inhibitors and useful in the treatment of cancer, inflammatory disorders and autoimmune disorders. The vast majority of this application is dedicated to the position that the heparanase inhibiting compounds disclosed therein have anti-proliferative activity, such as anticancer, inflammatory and in the treatment of autoimmune disorders. However, page 28 of *Ayal-hershkovitz et al.* does indicate a myriad additional disease states for the disclosed compounds, one of which is thrombocytopenia. The skilled worker would find no reason to believe the compounds of *Ayal-hershkovitz et al.* would be useful in enhancing proliferation from the disclosure or data in the specification. And no reason to believe that the compounds of *Ayal-hershkovitz et al.* would be useful in increasing platelet count.

Notwithstanding, the Examiner premises the rejection on the belief the all benzimidazole compounds belong to the same art recognized class, that both *Ayal-hershkovitz et al.* and Ajito et al. disclose benzimidazole compounds for use in treating thrombocytopenia, and thus the art reasonably suggest the benzimidazole compounds of Raeymaekers et al. are useful in the treatment of thrombocytopenia. Applicants cite *Ayal-hershkovitz et al.* and Ajito et al. for the premise that the pharmaceutical activity of benzimidazole compounds is a highly unpredictable art. The benzimidazole compounds of Ajito et al. decrease platelet activity while the benzimidazole compounds of *Ayal-hershkovitz et al.*, according to the Examiner, increase platelet activity. There is no disclosure in either of these references alone or in combination with *Raeymaekers et al.* that teaches or suggests how to alter the substituents on benzimidazole compounds in order to control which activity the compounds will exhibit. Further, there is no guidance in *Ayal-hershkovitz et al.* and/or Ajito et al. that would tell the skilled worker whether to expect platelet increasing activity or platelet decreasing activity, or heparanase inhibitory activity and/or άvβ3 antagonist activity and/or GP IIb/IIIa antagonist activity and/or TPO agonist activity by making the substituent changes on a benzimidazole ring that applicants have discovered in their current invention.

Ayal-hershkovitz et al., Ajito et al. and *Raeymaekers et al.*, alone or in combination with Raeymaekers et al., fail to provide the requisite motivation or desirability to prepare applicant's novel benzimidazole compounds with a high degree of probability of obtaining TPO agonist compounds that are useful in the treatment of thrombocytopenia. Absent the requisite motivation or desirability to prepare applicant's benzimidazole compounds the rejection here must be withdrawn.

Applicants submit that the references cited by the Examiner, alone or in combination, do not render their invention prima facie obvious and request that the rejection be withdrawn.

Applicants therefore submit that all reasons for rejection have been addressed and that the pending claims are allowable. Applicants respectfully request rejoinder of claims 55 and a Notice of Allowance. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned attorney at the number indicated below.

Respectfully submitted,

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